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21 T A E L E E S P E D S I Q L G V T R N K

atc atg aca gct caa tat gaa tgt tac caa aag att atg caa gac ccc att caa caa gca 180
41 I M T A Q Y E C Y Q K I M Q D P I Q Q A

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61 E G V Y C N R T W D G W L C W N D V A A

gga act gaa tca atg cag ctc tgc cct gat tac ttt cag gac ttt gat cca tca gaa aaa 300
81 G T E S M Q L C P D Y F Q D F D P S E K

ggt aca aag atc tgt gac caa gat gca aac tgg ttt aga cat cca gca agc aac aga aca 360
101 V T K I C D Q D G N W F R H P A S N R T

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121 W T N Y T Q C N V N T H E K V K T A L N

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141 L F Y L T I I G H G L S I A S L L I S L

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161 G I F F Y F K S L S C Q R I T L H K N L

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181 F F S F V C N S V V T I I H L T A V A N

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201 N Q A L V A T N P V S C K V S Q F I H L

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221 Y L M G C N Y F W M L C E G I Y L H T L

att gtg gtg gcc gtg ttt gca gag aag caa cat tta atg tgg tat tat ttt ctt ggc tgg 780
241 I V V A V F A E K Q H L M W Y Y F L G W

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261 G F P L I P A C I H A I A R S L Y Y N D

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281 N C W I S S D T H L L Y I I H G P I C A

gct tta ctg gtg aat ett ttt ttc ttg tta aat att gta cgc gtt ctc atc acc aag tta 960
301 A L L V N L F F L L N I V R V L I T K L

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321 K V T H Q A E S N L Y M K A V R A T L I

ttg gtg cca ttg ctt ggc att gaa ttc gtg ctg att cca tgg cga cct gaa gga aag att 1080
341 L V P L L G I E F V L I P W R P E G K I

gca gag gag gta tat gac tac atc atg cac atc ctt atg cac ttc cag ggt ett ttg gtc 1140
361 A E E V Y D Y I M H I L M H F Q G L L V

tct acc att ttc tgc ttc ttt aat gga gag gtt caa gca att ctg aga aga aac tgg aat 1200
381 S T I F C F F N G E V Q A I L R R N W N

caa tac aaa atc caa ttt gga aac agc ttt tcc aac tca gaa gct ett cgt agt gcg tct 1260
401 Q Y K I Q F G N S F S N S E A L R S A S

tac aca gtg tca aca atc agt gat ggt cca ggt tat agt cat gac tgt cct agt gaa cac 1320
421 Y T V S T I S D G P C Y S H D C P S E H

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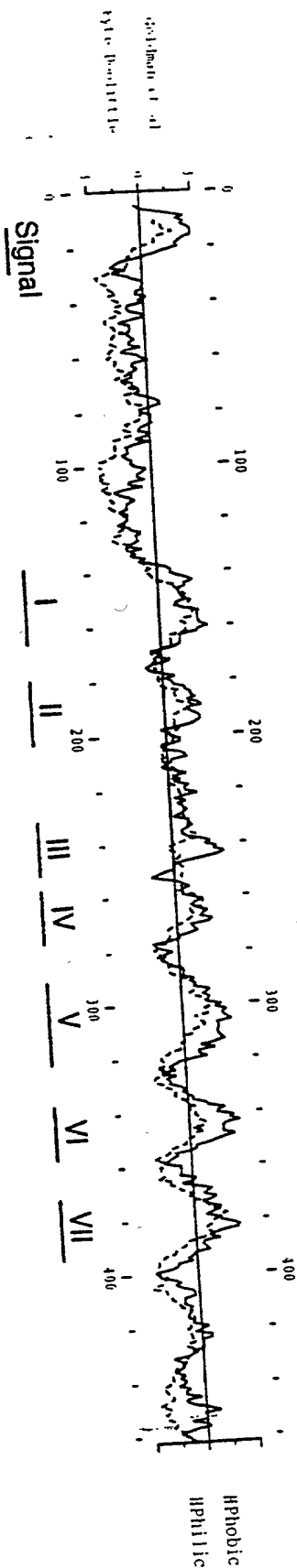
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FIGURE 1

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Hydropathy Plot of the Human CGRP Receptor Peptide Sequence



325800-376

F760KE 2

10651135 012202

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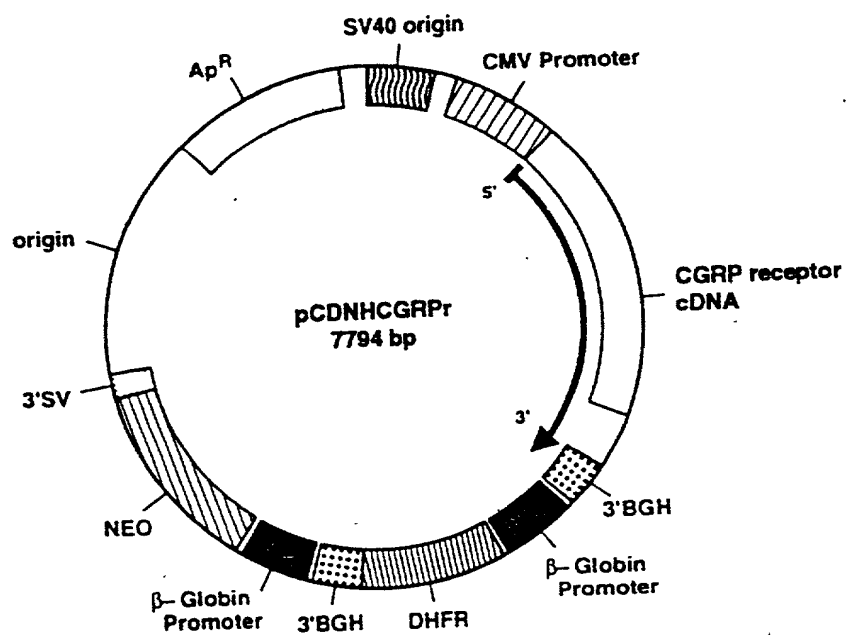


FIGURE 3

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cAMP RESPONSE IN 293 CELLS

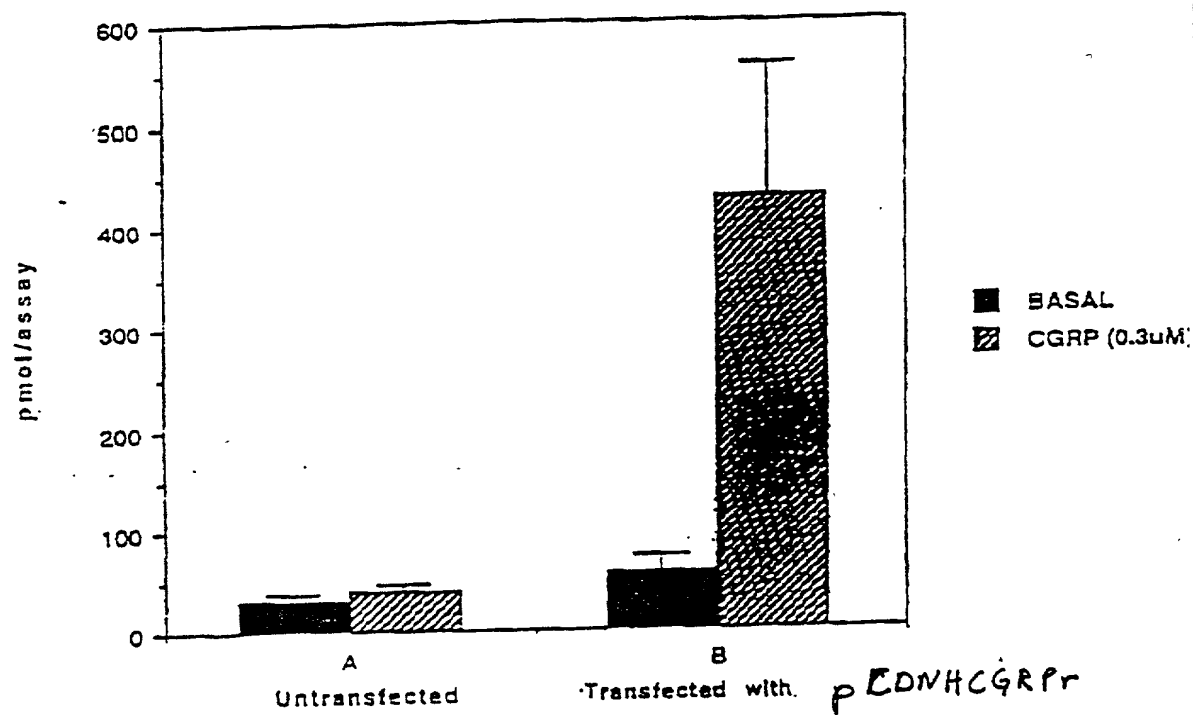


FIGURE 4

325000 376

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EFFECT OF CGRP
TREATMENT OF 293 CELL LINES STABLY TRANSFORMED WITH THE
pCONHCGRP CONSTRUCT

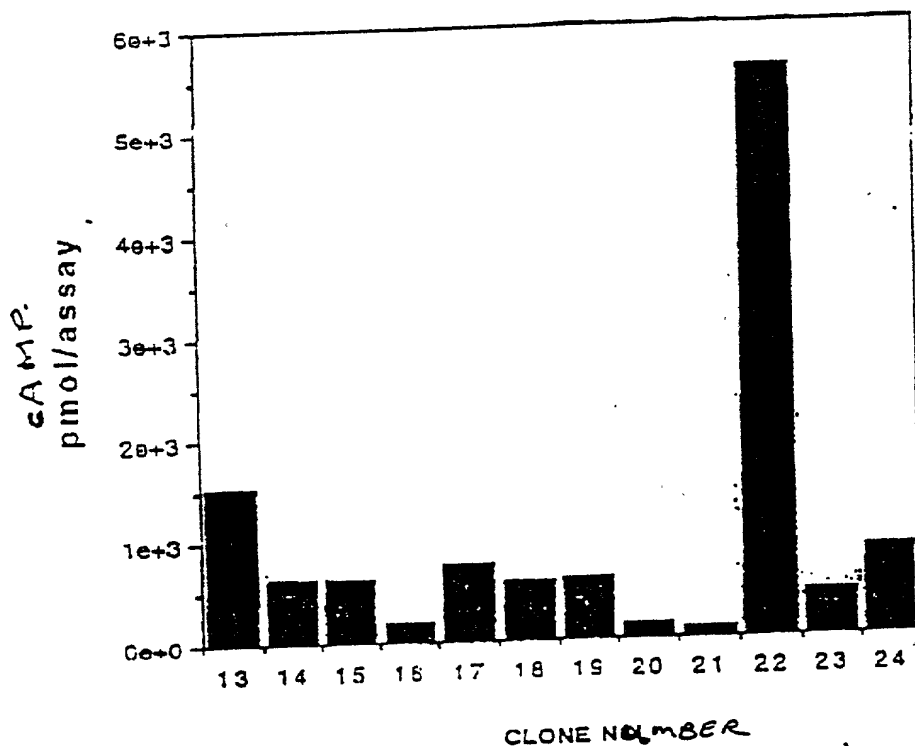


FIGURE 5

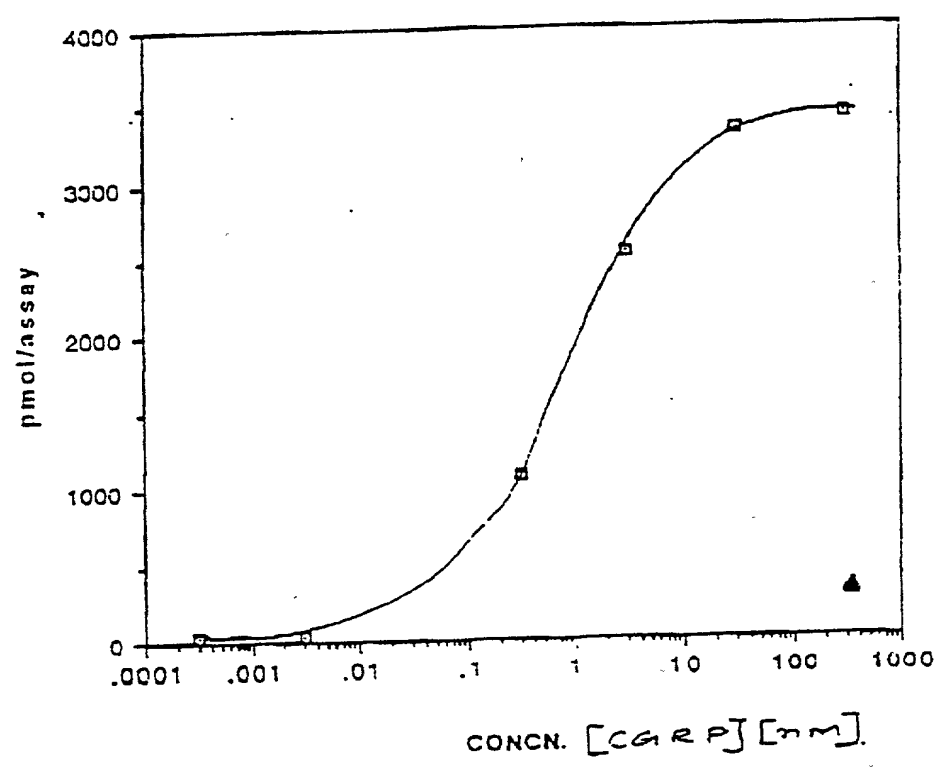
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pCDN#CGRP

CGRP-MEDIATED cAMP IN

STABLY TRANSFORMED 293 CELLS (CLONE 22)



□ Transfected
▲ Untransfected cells.

FIGURE 6

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EFFECT OF CGRP8-37 ON CGRP-MEDIATED cAMP IN pCDNHGGRPr STABLY TRANSFORMED 293 CELLS (CLONE 22)

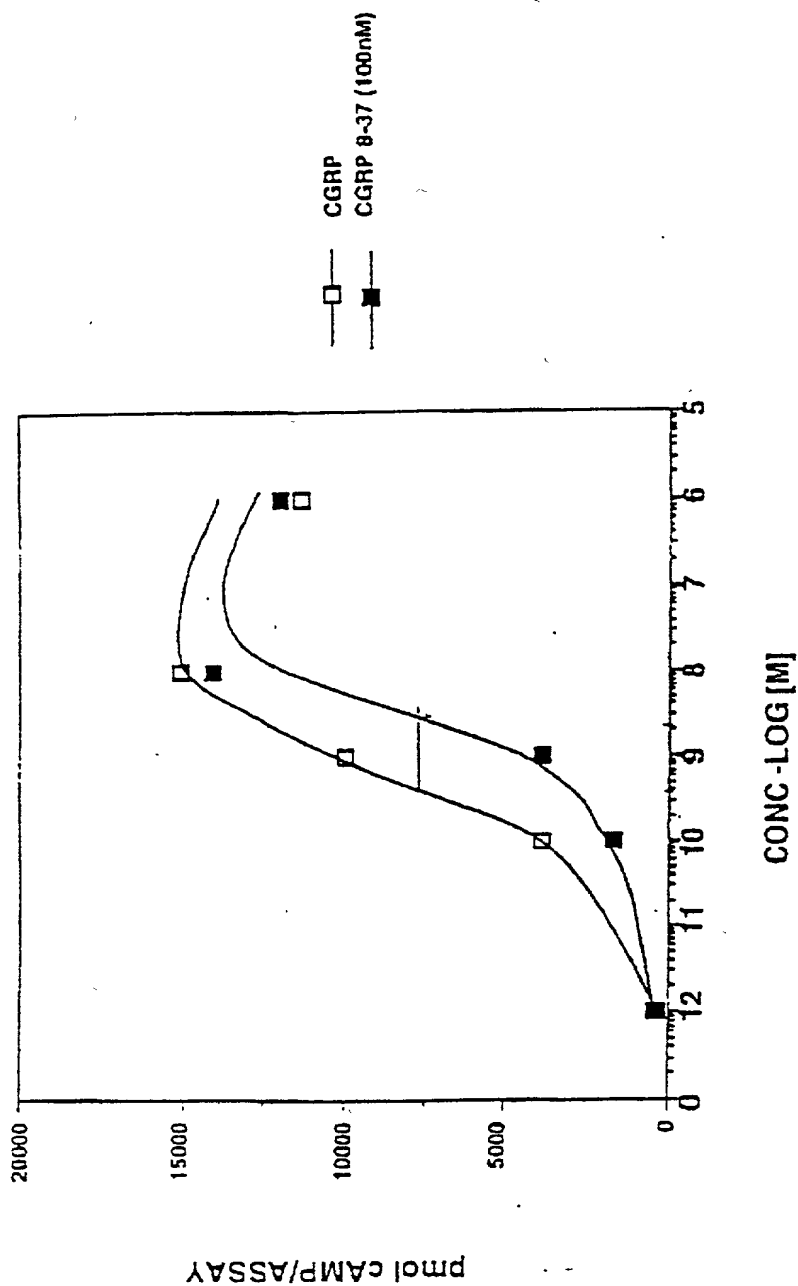


FIGURE 7

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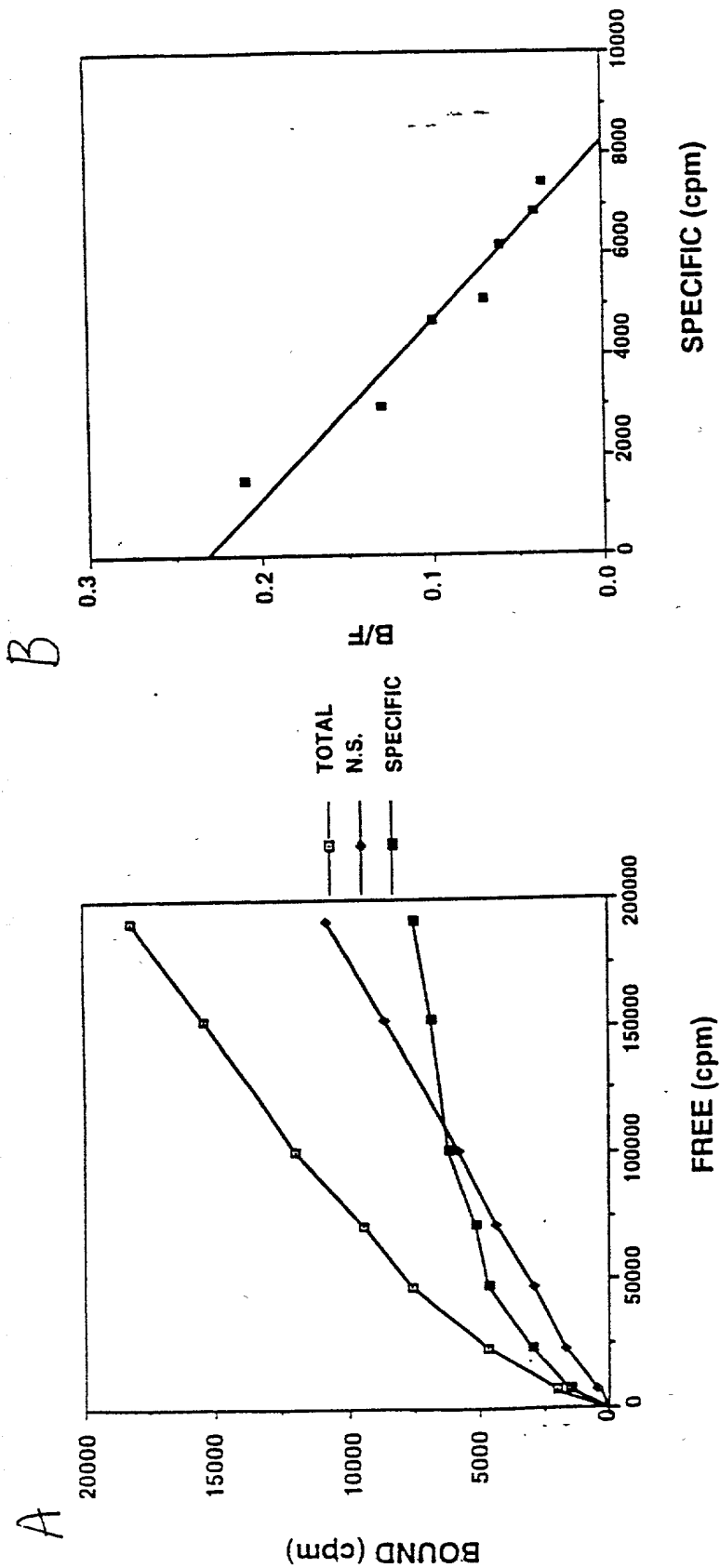


FIGURE 8

COMPETITION CURVES FOR REPRESENTATIVE CGRP ANALOGS
AGAINST [125I]CGRP BINDING IN pCDNHCGRP TRANSFORMED CELL (CLONE 22) MEMBRANES

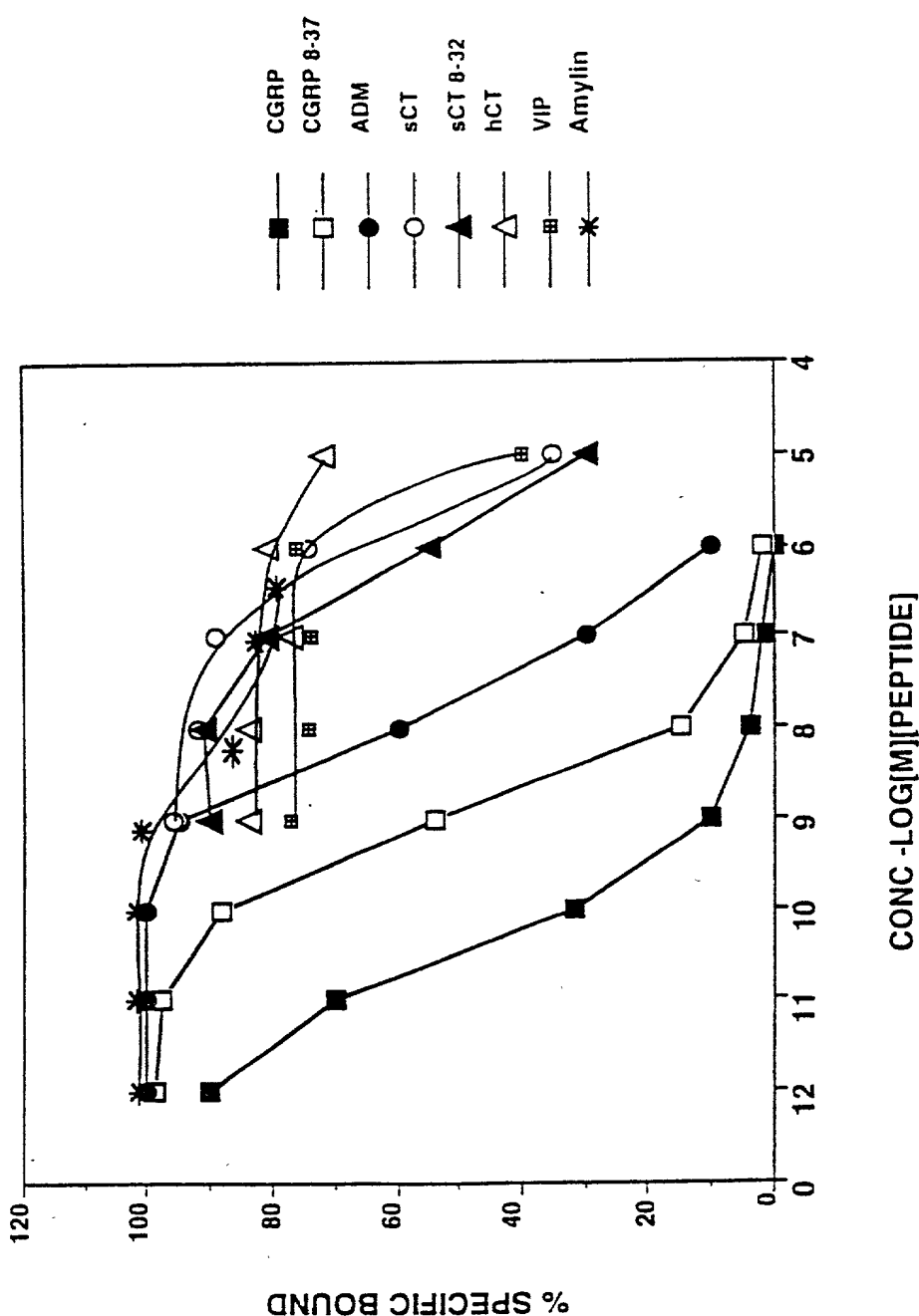


FIGURE 9
CGRP > CGRP 8-37 > ADM > sCT 8-32 > sCT > VIP > Amylin, hCT

30560-376

Comparison of Human CGRP and Human Calcitonin Receptor Amino Acid Sequences

1MEKKCTLYFLVL...LPFFMILVTAELEESPEDSIQLGVTRNKIMT 43
 1 MRFTFTSRCLALFLLLNHPTILPAFSNQTYPTIEPKPFLYVVGRRKKMMD -50
 44 AQYECYQKIMQDPIQQAEGVYCNRTWDGWLCWNDVAAGTESMQLCPDYFQ 93
 51 AQYKCYDRNQQLPAYQGEPTCNRTWDGWLCWDDIPAGVLSTQFCPDYFF 100
 94 DFDPSEKVTKICDQDGNWFRHPASNRTWTNYTQCNVNTHEKVKTALNLFY 143
 101 DFDPSEKVTKYCDEKGVWFKHPENNRTWSNYTMCNAFTPEKLNAYVLYY 150
 144 LTIIGHGLSIASSLISLGIFYFK.....SLSCQRITLH 177
 151 LAIVGHSLSIFTLVISLGIFVFFRKLTTIFPLNWKYRKALSLGCQRVTLH 200
 178 KNLFFSFVCNSVVTIIHLTAVANNQALVATNPVSCKVSQFIHLYLMGCNY 227
 201 KNMFLTYILNSMIIIIHLVEVVPNGELVRRDPVSKILHFFHQYMMACNY 250
 228 FWMLCEGIYLTILVAVFAEKQHLMWYFLGWGFPLIPACIHAIARSLY 277
 251 FWMLCEGIYLTILVAVFTEKQRLRWYLLGWGFPLVPTTIHAITRAVY 300
 278 YDNCWISSDTHLLYIIHGPICAALLVNLFLLNIVRVLITKLKVTHQAE 327
 301 FNDNCWLSVETHLLYIIHGPMMAALVVNFFLLNIVRVLVTKMRETHEAE 350
 328 SNLYMKAVRATLILVPLLGIEFVLIPIWRPEGKIAEEVDYIMHILMHFQG 377
 351 SHMYLKAVKATMILVPLLGIFVVPWRPSNKMGLGKIYDYVMHSLIHFGQ 400
 378 LLVSTIFCFFNGEVQAILRRNWNQYKIQFGNSFSNSEALRSASYTVSTIS 427
 401 FFFVATIIYCFNCNEVQTTVKRQWAQFKIQWNQRWGRRPSNRSARAAAAAAE 450
 428 DGPGYSHDCPSEHLNGKS.IHDIENVLLKPENLYN..... 461
 451 AGDIPYICHQEPRNEPANNOGEESAEIIPLNIEQESSA 490

FIGURE 10

Comparison of Human and Rat CGRP Receptor Amino Acid Sequences

1 MEKKCTLYFLVLLPFFMILVTAEELESPEDSIQLGVTRNKIMTAQYECY 49
 1 MMDKKCTLCFLFLLLLNMALIAAESEEGANQT.DLGVTRNKIMTAQYECY 49
 50 QKIMQDPIQQAEGVYCNRTWDGWLWCWNDVAAGTESMQLCPDYFQDFDPSE 99
 50 QKIMQDPIQQEGLYCNRTWDGWLWCWNDVAAGTESMQLCPDYFQDFDPSE 99
 100 KVTIKCDQDGNWFRHPASNRWTWNTYTQCNVNTHEKVKTAIENLFYLTIIIGH 149
 100 KVTIKCDQDGNWFRHPDSNRWTWNTYTLCNNSTHEKEKTAIENLFYLTIIIGH 149
 150 GLSIASLLISLGIFFFYFKSLSCQRITLHKNLFFSFVCNSVVTIIHLTAVA 199
 150 GLSIASLLISLIIFFFYFKSLSCQRITLHKNLFFSFVCNSIVTIIHLTAVA 199
 200 NNQALVATNPVSCKVSQFIHLYLMGCNYFWMLCEGIYLTIVVAVFAEK 249
 200 NNQALVATNPVSCKVSQFIHLYLMGCNYFWMLCEGIYLTIVVAVFAEK 249
 250 QHLMWYFFLGWGFPLIPACIHAIARSLLYNDNCWISSDTHLLYIIHGPIK 299
 250 QHLMWYFFLGWGFPLIPACIHAIARSLLYNDNCWISSDTHLLYIIHGPIK 299
 300 AALLVNLFLLNIVRVLITKLKVTHQAESNLYMKAVRATLILVPLLGEF 349
 300 AALLVNLFLLNIVRVLITKLKVTHQAESNLYMKAVRATLILVPLLGEF 349
 350 VLIPWRPEGKIAEEVYDYIMHILMHFQGLLVSTIFCFFNGEVQAILRRNW 399
 350 VLFPWRPEGKVAEEVYDYVMHILMHYQGLLVSTIFCFFNGEVQAILRRNW 399
 400 NQYKIQFGNSFSNSEALRSASYTVSTISDGPYSHDCPSEHLNGKSIHDI 449
 400 NQYKIQFGNGFSHSDALRSASYTVSTISDVQGYSHDCPTEHLNGKSIQDI 449
 450 ENVLLKPENLYN... 461
 450 ENVALKPEKMYDLVM 464

FIGURE 11